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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,396	06/16/2005	Tang Lan	10348.204-US	6758

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EXAMINER	
RAGHU, GANAPATHIRAM	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/539,396	LAN ET AL.	
	Examiner	Art Unit	
	Ganapathirama Raghu	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/16/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 30-49 are pending in this application and are under consideration for examination.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). This application is a 371 of PCT/DK03/00882 filed on 12/16/2003 and claims the priority date of Denmark application PA 2002 01928 filed on 12/17/2002.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 06/16/2005 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

The drawings are considered for examination purposes only.

Specification

The use of the trademarks through out the specification, for e.g., pages 18-19, 21, has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 48 and dependent claim 49 are rejected under 35 U.S.C. 101 because the claim could read on a non-statutory subject matter. The claim is drawn to a 'A recombinant host cell...', which could be an integral part of a human being. Claims directed to such matter are considered non-statutory. Examiner suggests amending the claim to recite 'An isolated recombinant host cell' in order to overcome the rejection.

Claim Rejections: 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 30 and claims 31-49 depending therefrom, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 30-32, 34-35, 37-38, 40-41 and 43-45 recite the phrase "...comprising an amino acid sequence...", as the metes and bounds are not clear to the Examiner. It is not clear whether the claims encompass a polypeptide comprising

a fragment or a sub sequence of the polypeptide that is 8% identical to amino acids 22-450 of SEQ ID NO: 4 or polypeptides comprising the full length of amino acid sequence that are 80% identical to SEQ ID NO: 4. Examiner suggests amending the claim to recite "...comprising the amino acid sequence...".

Claim 30 and claims 31-49 depending therefrom, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 30, 33, 36, 39, 42 and 45-46 recite the phrase "... encoded by a polynucleotide comprising a nucleotide sequence...", as the metes and bounds are not clear to the Examiner. It is not clear whether the claims encompass the full-length sequence comprising the nucleic acid sequence shown from position 68-1417 of SEQ ID NO: 3 or any portion, fragments of sequence from position 68-1417 SEQ ID NO: 3. In order for the full-length of the polynucleotides to be encompassed in said sequences, Examiner suggests amending the claims to read as "...comprising the polynucleotide sequence...". Clarification is required.

Claim 30 and claims 31-49 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 30-32, 34-35, 37-38 and 40-41, recites the phrase "...80% identity with amino acids 22-450 of SEQ ID NO: 4..." or "...85% identity with amino acids 22-450 of SEQ ID NO: 4..." or "...90% identity with amino acids 22-450 of SEQ ID NO: 4 "...95% identity with amino acids 22-450 of SEQ ID NO: 4...", the metes

and bounds of the phrase is not clear and the Examiner suggests changing the phrase to "...80% sequence identity or 85% sequence identity or 90% sequence or 95% sequence identity with amino acids 22-450 of SEQ ID NO: 4..." and so on for the respective claims.

Claim 30 and claims 31-49 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 30, 33, 36, 39 and 42 recite the phrase "...80% identity with the sequence shown from position 68-1417 in SEQ ID NO: 3..." or "...85% identity with the sequence shown from position 68-1417 in SEQ ID NO: 3..." or "...90% identity with the sequence shown from position 68-1417 in SEQ ID NO: 3 "...95% identity with the sequence shown from position 68-1417 in SEQ ID NO: 3...", the metes and bounds of the phrase is not clear and the Examiner suggests changing the phrase to "...80% sequence identity or 85% sequence identity or 90% sequence or 95% sequence identity with the sequence shown from position 68-1417 in SEQ ID NO: 3..." and so on for the respective claims.

Claim 30 and claims 31-49 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 30, 33, 42, 45 recites the phrase "...shown from... SEQ ID NO:..". It is not clear to the Examiner as to what this phrase means in the context of the above claims. It is not clear whether the isolated polypeptide or polynucleotide indeed actually has the sequence 22-450 of SEQ ID NO: 4 or 68-1417 of SEQ ID NO: 3 respectively or whether SEQ ID NO: 4 or SEQ ID NO: 3 is a representative sequence of the

isolated polypeptide or polynucleotide. Examiner suggests applicant to make a direct reference to the SEQ ID NO: 4 or SEQ ID NO: 3 such as "...polypeptide sequence from position 22-450 of SEQ ID NO: 4 or "...polynucleotide sequence from position 68-1417 of SEQ ID NO: 3".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 30 and claims 31-49 depending therefrom are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 30 recites a genetically modified *E. coli* strain deposited under Budapest Treaty with DSMZ under accession number DSM 15334.

It is apparent that *E. coli* strain DSM 15334is required to practice the claimed invention. As such the biological material must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 USC112, first pargraph, may be satisfied by a deposit of the *E. coli* strain DSM 15334.

It is noted that applicants have deposited the organism under the terms of Budapest Treaty but there is no indication in the specification as to the public availability. Since the deposit was made under the terms of Budapest Treaty, a statement, affidavit or declaration by Applicants, or a statement by an attorney of record over his/her signature and registration

number, or someone empowered to make such a statement, stating that the invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. The applicant must submit a statement from a person to corroborate the fact, stating that the biological material specifically identified in the application as filed.

Claim 30 and claims 31-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding a polypeptide with amino acids 22-450 of SEQ ID NO: 4 having alpha amylase activity and the encoding polynucleotide with nucleic acid sequence from position 68-1417 of SEQ ID NO: 3, vectors, isolated host cells comprising the polynucleotide and a method of making the polypeptide, does not reasonably provide enablement for any polynucleotide encoding a polypeptide having 80%-95% amino acid sequence identity with amino acids 22-450 of SEQ ID NO: 4 and said polynucleotide having 80%-95% nucleic acid sequence identity with nucleic acid sequence from position 68-1417 of SEQ ID NO: 3, vectors, isolated host cells and a method of making said polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 30-49 are so broad as to encompass any polynucleotide encoding a polypeptide having 80%-95% amino acid sequence identity with amino acids 22-450 of SEQ ID NO: 4 and said polynucleotide having 80%-95% nucleic acid sequence identity with nucleic acid sequence from position 68-1417 of SEQ ID NO: 3, vectors, isolated host cells and a method of making said polypeptide. The scope of the claims are not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides and encoded polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide sequence of only one polynucleotide with SEQ ID NO: 3 from position 68-1417 encoding the polypeptide with amino acids 22-450 of SEQ ID NO: 4 having alpha amylase activity. It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides and that are simply 80%-95% identical to SEQ ID NO: 3 from position 68-1417 or polynucleotides encoding an amino acid sequence that has 80%-95% sequence identity with amino acids 22-450 of SEQ ID NO: 4 and having alpha amylase activity. The specification is limited to teaching the use of SEQ ID NO: 3 from position 68-1417

encoding the polypeptide with amino acids 22-450 of SEQ ID NO: 4 having alpha amylase activity, but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make and use the claimed polynucleotides and polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide encoding a polypeptide having 80%-95% amino acid sequence identity with amino acids 22-450 of SEQ ID NO: 4 and said polynucleotide having 80%-95% nucleic acid sequence identity with nucleic acid sequence from position 68-1417 of SEQ ID NO: 3, vectors, isolated host cells and a method of making said polypeptide,

because the specification does not establish: (A) a rational and predictable scheme for modifying specific nucleotide in the polynucleotide encoding the polypeptide with SEQ ID NO: 2 with an expectation of obtaining the desired biological function, i.e., alpha amylase activity; (B) Modifications of specific amino acids in SEQ ID NO: 2 without affecting the alpha amylase activity, (C) the general tolerance of said polynucleotides and polypeptides to modification and the extent of such tolerance without affecting the activity of said polynucleotides or encoded polypeptides, (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claim broadly including polynucleotides and polypeptides with an enormous number of modifications. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides and polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached on 8 am - 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached

on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ganapathirama Raghu, Ph.D.
Patent Examiner
Art Unit 1652

Mar. 10, 2006.